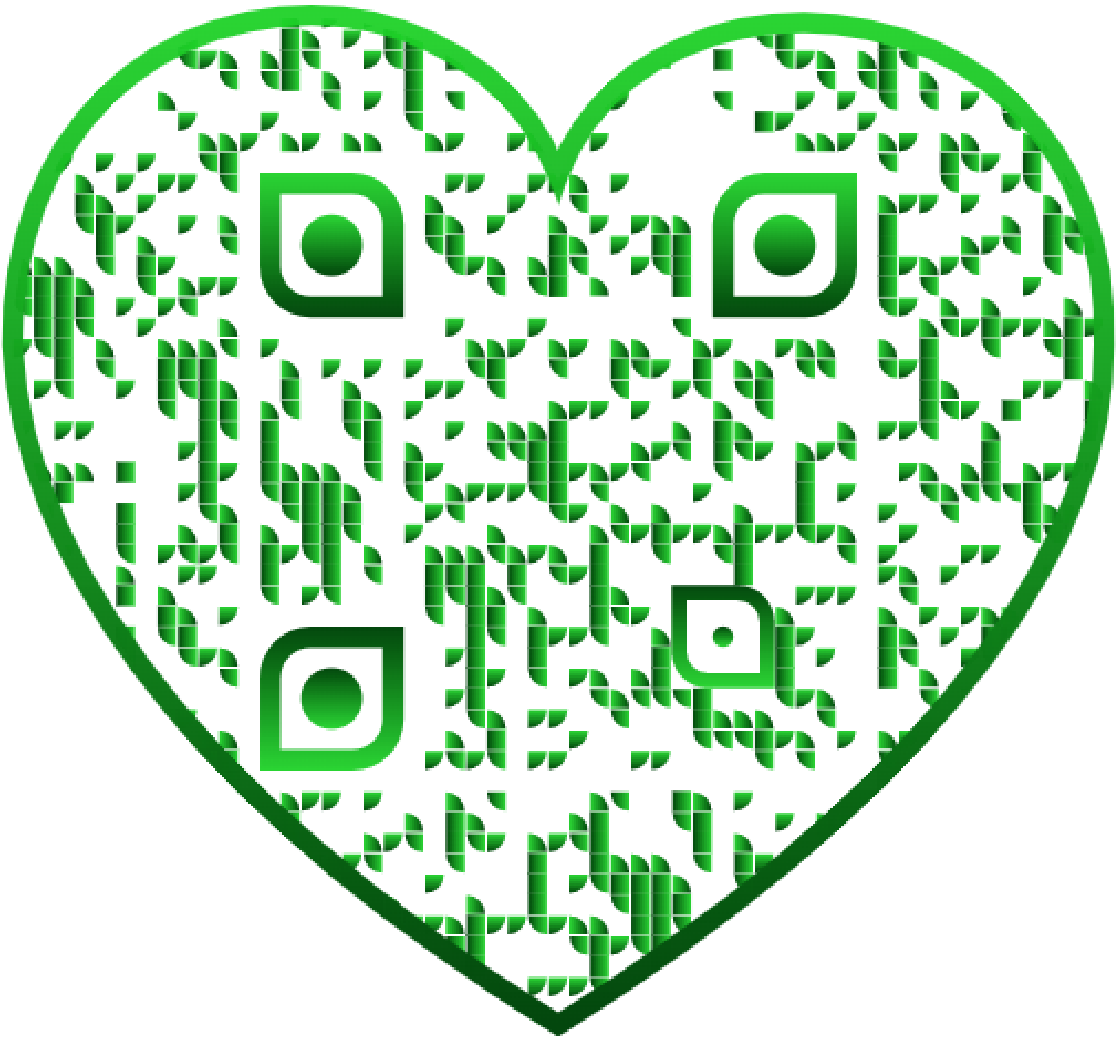
Organic Chemistry ll

Stereochemistry

Lamia Alorabi



1 1 / /

Stereochemistery :- Chemistery of 3D of chemical molecular, it's the heart of chemistery, and study the depth of compound.

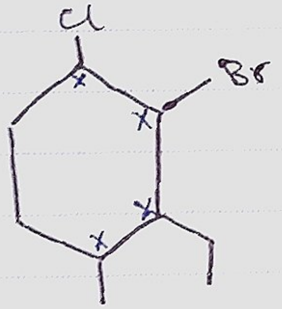
3D ⇒ front and back
2D ⇒ right and left.

3D ⇐ كيمياء ثلاثية الأبعاد.

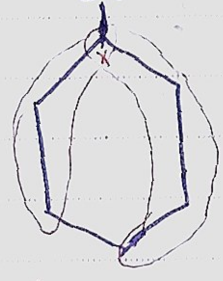
Chiral : A carbon atom which attached with four different group.

* ليست كل المركبات Chiral
* لا يستطيع فصل Chiral طبيعياً إلا الإنسان والنبات والحيوان.
* كل Chiral يحتوي على إثنين أيزومر.
* في الأحماض الدهنية يكون الأيزومر عبارة عن ⇐ L
* في الكربوهيدرات يكون الأيزومر عباره عن ⇐ D
* الأيزومر إما يكون Chiral أو Double.

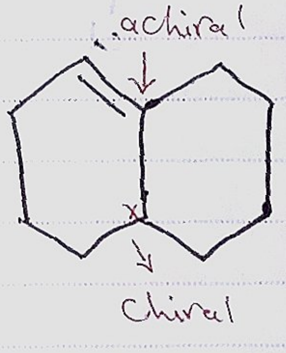
* Determine the chirality :-



4 - chiral
16 - isomer



1- Chiral
2- isomer

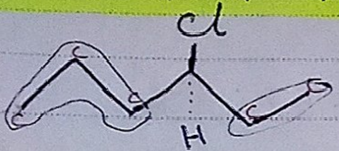


- إذا وجد Double لا يعتبر Chiral
- أي حلقتين متصلتين غير البنزين الكربونتين التي في الوسط → Chiral

أصنع الحضارة

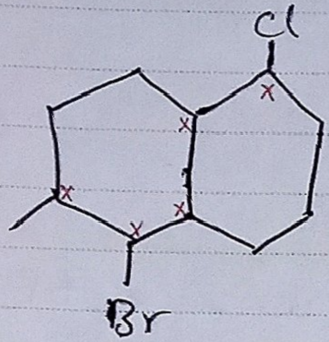
1

2 ١ ١



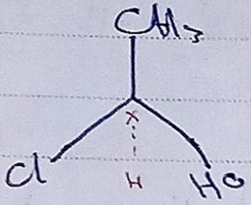
⇒ chiral

* الكـــربونة الطرفية لاتعتبر chiral

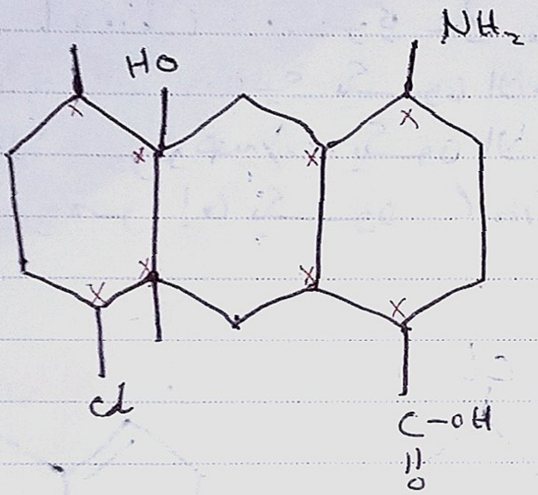


⇒ 5 chiral , isomer = $2^5 = 32$

chiral عدد = n ⇐ 2^n = isomer *



⇒ chiral



⇒ 8 chiral

2^8 isomer = 256

اصنع الحضارة

2

3 / /

* Isomer ⇒ Compounds that have the molecular formula, but different molecular structural.

- Molecular formula ⇒ is the type and number of atoms.
- Molecular structure ⇒ Bonds in the Compounds.

ex. CH_3CH_2CHO ⇔ compound

CH_3-O-CH_3 ⇐ isomers ⇒ CH_3COCH_3

Isomer

(تركيبي)

Structural or Constitutional

⇓

Different in physical chemical and name.

⇓ (مثال) مثال/

① $CH_3-CH_2-\overset{O}{\overset{\|}{C}}H$

② $CH_3-\overset{O}{\overset{\|}{C}}-CH_3$

المركب الاول ألدهيد والثاني كيتون لهما نفس الصيغة الكيميائية

-- C_3H_6O --

لكن مختلفان بالتركيب فيسمى

-- structural --

(ثلاثي الابعاد)

Stereoisomer

⇓

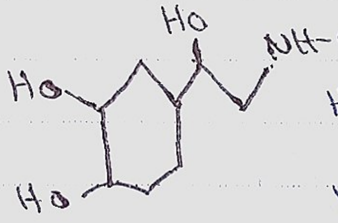
The same in physical chemical and name

⇓

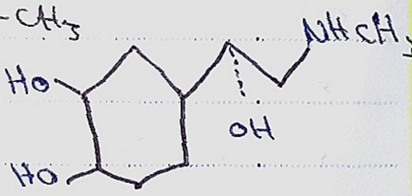
يكون الاختلاف فقط بالتوجيه، واحد أمام والثاني خلف.

⇓ (مثال)

الأدرينالين يمتلك ٢ أيزومر أمام وخلف



(أمام)



(خلف)

2

4 / /

Stereoisomer

Configuration

- high energy barrier
- it's chiral

تتحرك ٤ ذرات المرتبط ب C
باتجاهين أمام وخلف وإذا
كانت cis and trans

- asymmetric
- sterogenic center

Conformation

- low energy barrier
- it's achiral

تتحرك ذرة C بحرية
في كل الاتجاهات

- symmetric

ينقسم إلى نصفين
بشكل متساوي

Configuration

enantiomer

① Mirror image not superimpose

(صورة لبعضهما من غير تطابق)

① The same physical chemical properties but differen in biological activity

(المفعول)

مثال / الأدرينالين

diasteromer

① not mirro image

② not superimpose

(لا صورة ولا تطابق)

③ Different in physical chemical and biological

[٢]

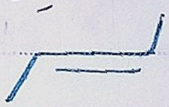
5 / ٠ /

[redacted] chiral يظهر في الواحد ⇐ enantiomer

أو أكثر Chiral يظهر في الإثنين ⇐ diasteromer

Configuration

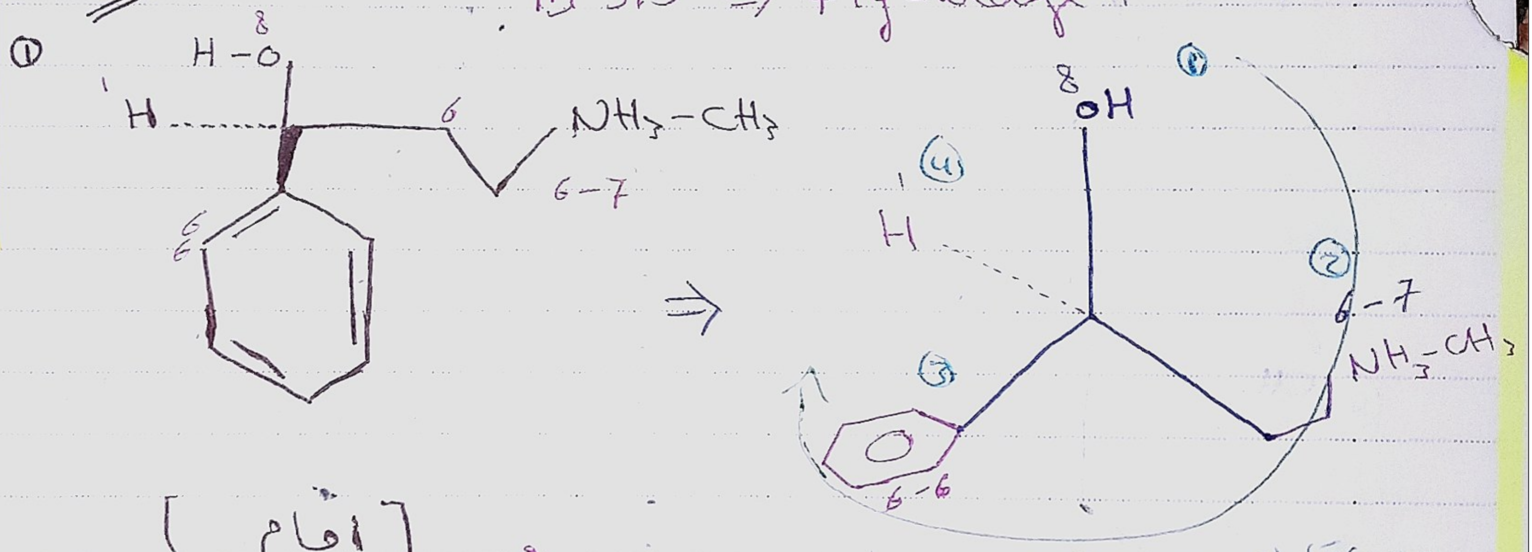
- Optical activity
  - enantiomer
  - diasteromer
- Geometric
  - (مع.) Cis ⇓ في إتجاه واحد
  - (ضد.) Trans ⇓ إتجاهين مختلفين



* Representative of isomer (رسم الأيزومرات) :-

مثال 1

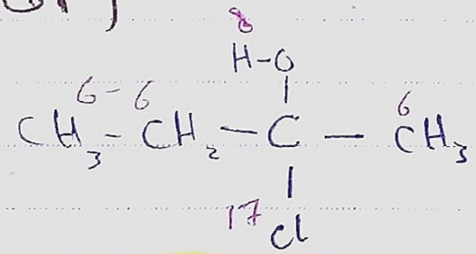
[1] 3D ⇒ fly-wedge :


①
8
H − O
1
H
6
NH3 − CH3
6 − 7
6
6
⇒
8
OH
1
H
④
①
②
6 − 7
NH3 − CH3
③
6 − 6

[أقام]

R ⇒ مع عقارب الساعة الإتجاه

(مثال 2)



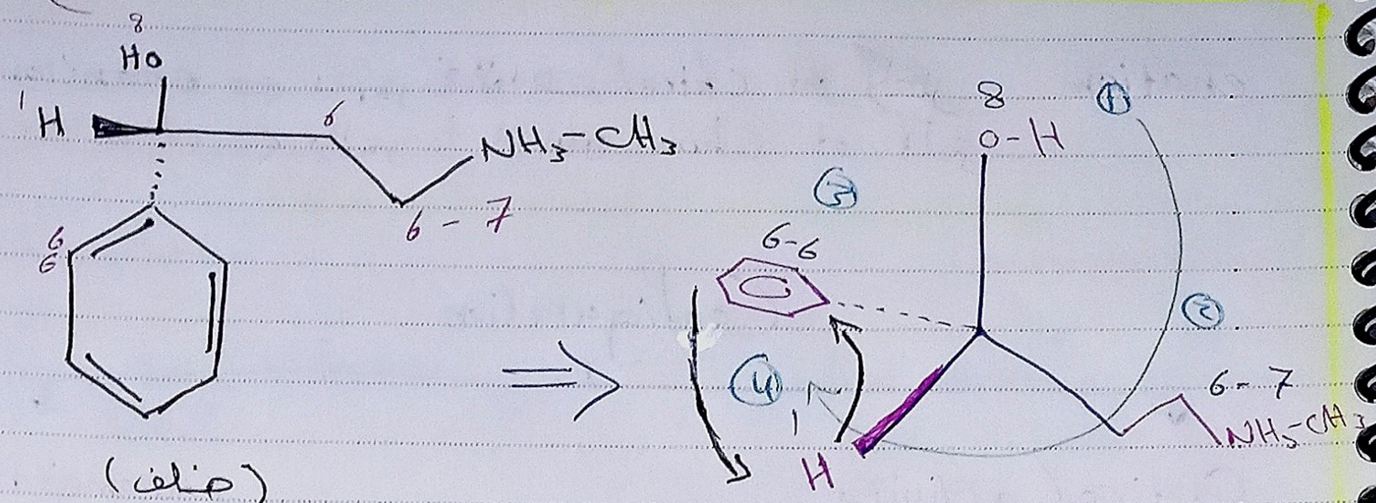
$$CH_3 - CH_2 - \overset{\overset{8}{H-O}}{\underset{\underset{17}{Cl}}{C}} - CH_3$$

صنو الحضارة

[2]

تابع مثال 1:

⇒


8
Ho
1
H
6
NH3-CH3
6 - 7
6
6
8
O-H
①
③
6-6
②
④
1
H
6-7
NH3-CH3

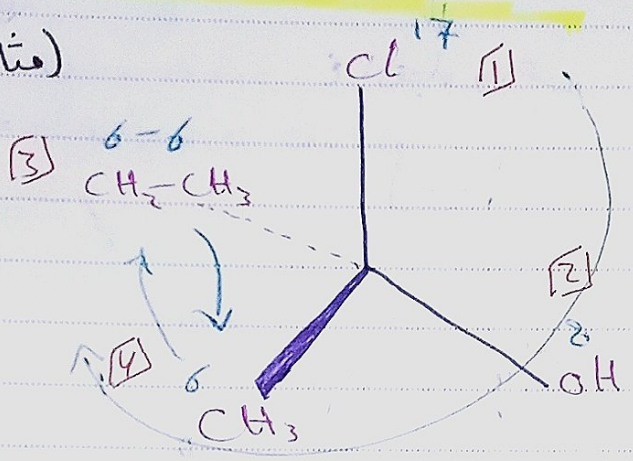
(ضلف)

R → S

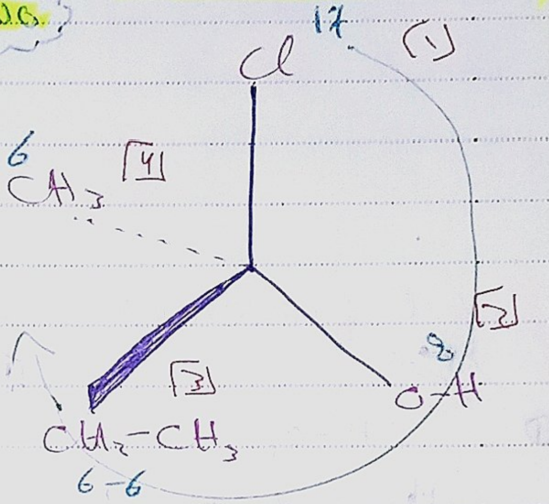
* الاتجاه بيكون مع عقارب الساعة لكن بالأصل عكس عقارب الساعة

In vivo

(مثال 2)

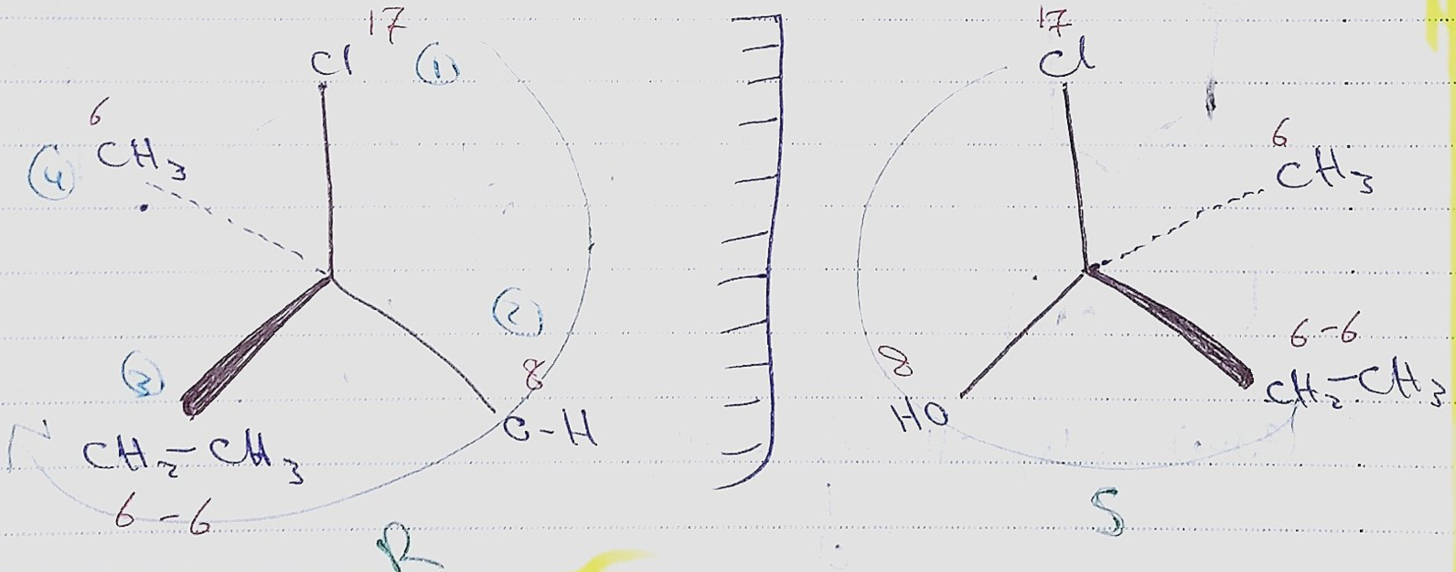

Cl
17
[1]
[3]
6-6
CH2-CH3
[2]
8
O.H
[4]
6
CH3

R → S


Cl
17
(1)
6
CH3
[4]
[2]
8
O-H
[3]
CH2-CH3
6-6

R

In vitro


17
Cl
①
6
④
CH3
②
③
8
O-H
CH2-CH3
6-6
17
Cl
6
CH3
8
HO
6-6
CH2-CH3

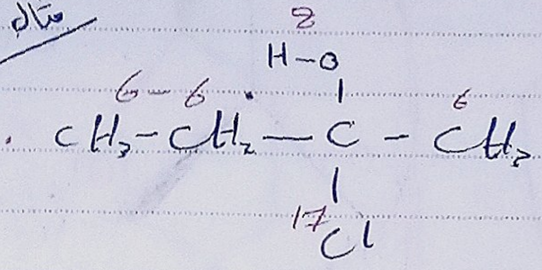
R

S

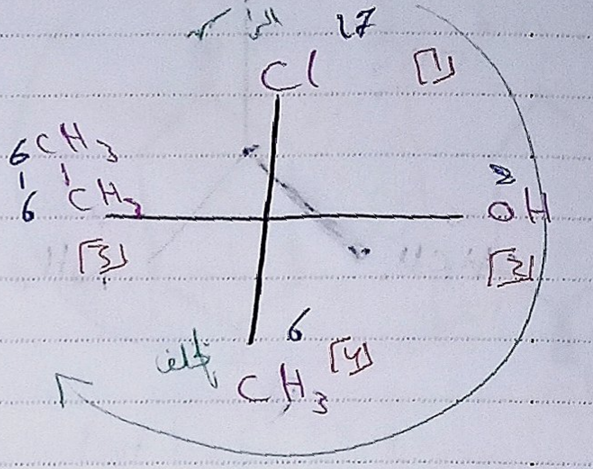
* Represenation of isomer :

[2] 2D ⇒ fisher projections

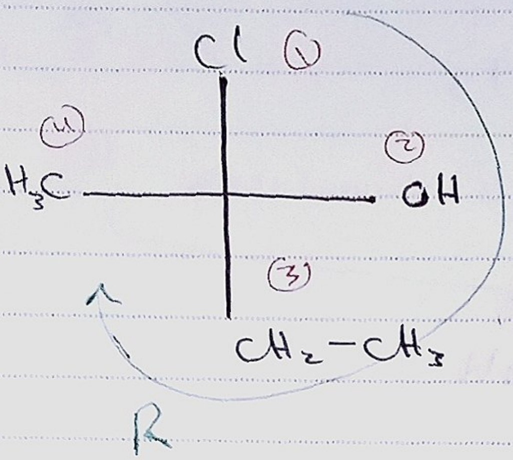
مثال


$CH_3-CH_2-\underset{Cl}{\overset{H-O}{C}}-CH_3$

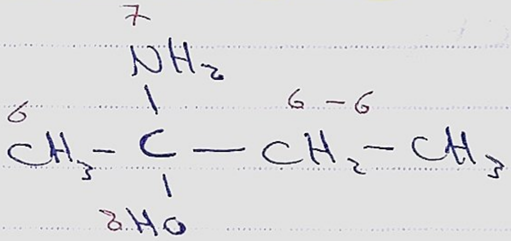
⇒


17
Cl
[1]
6 CH3
6 CH3
[3]
8
OH
[2]
6
CH3
[4]

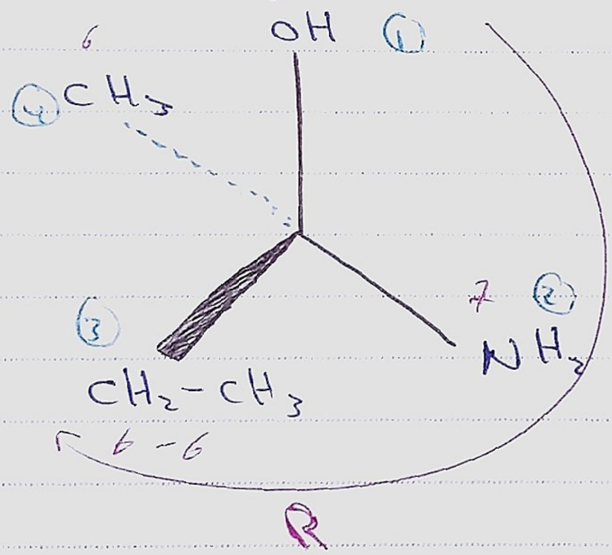
R → S clockwise

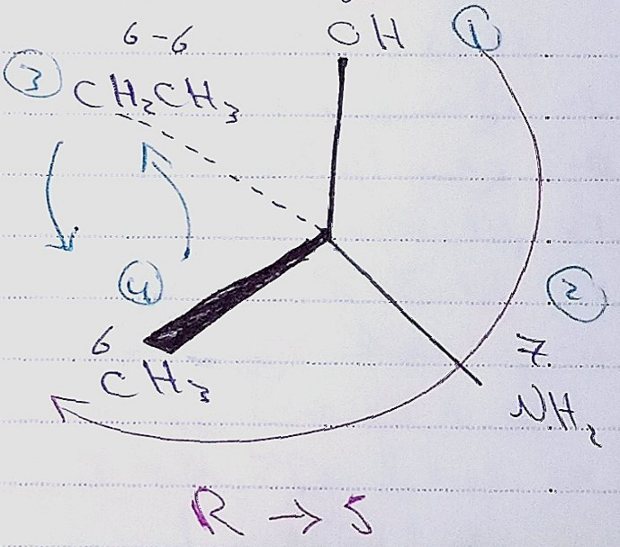

Cl
①
④
②
H3C
OH
③
CH2 – CH3
R

مثال


$CH_3-\underset{HO}{\overset{NH_2}{C}}-CH_2-CH_3$

⇓


8
OH
①
6
④ CH3
7
②
NH2
③
CH2 – CH3
6 – 6
R

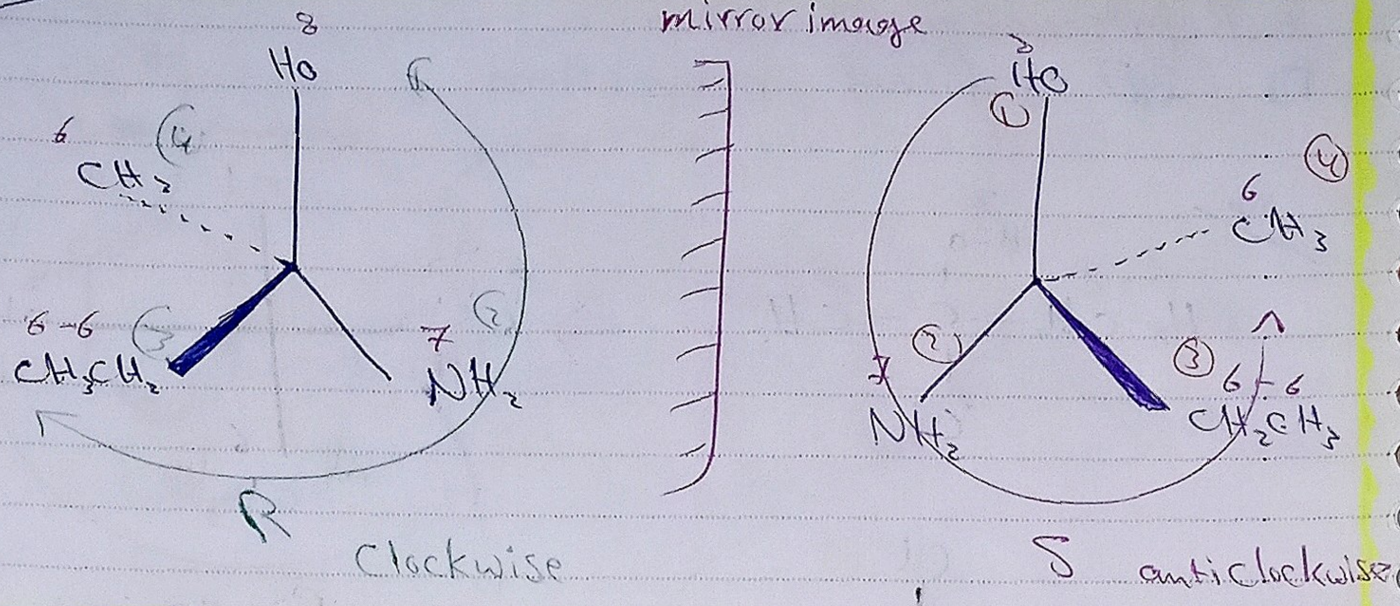

8
6 – 6
OH
①
③ CH2CH3
④
②
6
CH3
7
NH2
R → S

مينو الحضارة

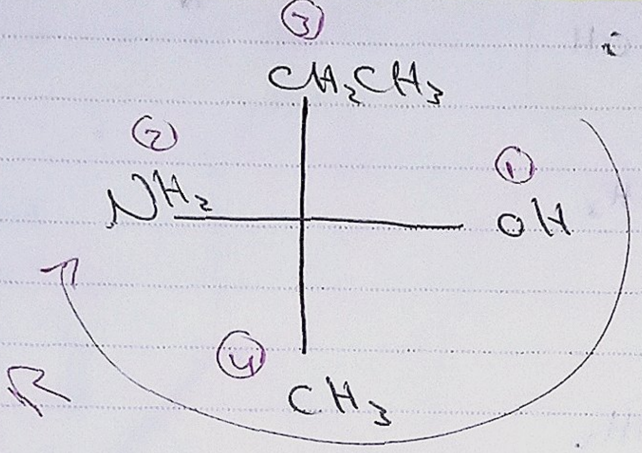
2

8 / /

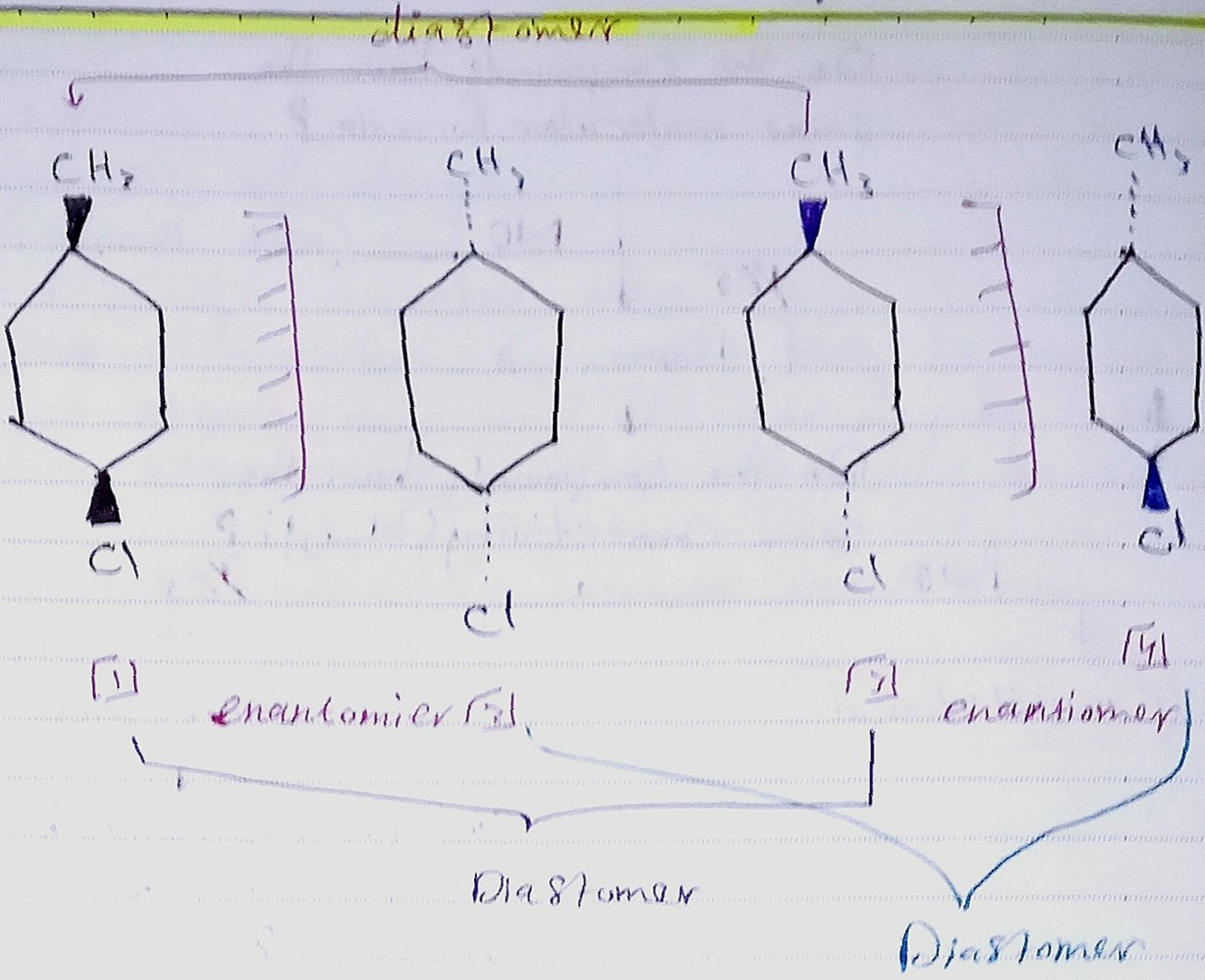
تابع مثال


mirror image
8
Ho
4
6
CH3
6 - 6
3
CH3CH2
7
2
NH2
R
Clockwise
HO
1
4
6
CH3
2
7
NH2
3
6 - 6
CH2CH3
S
anticlockwise

2D


3
CH2CH3
2
NH2
1
OH
4
CH3
R

صنع الحضارة


diastomer
CH3
Cl
[1]
[2]
[3]
[4]
enantomier
enantiomer
Diastomer
Diastomer

* خطوات تمثيل الأيزومر:

١- نكتب أكبر عدد ذري في كل مركبا

٢- العدد الذري الأكبر يعتبر الرأس ويكتب بالأعلى

٣- العدد الذري الأصغر يعتبر الخلف ونعبر عنه بالداش في 3D أما في 2D فيكون عمودي في الأسفل.

٤- نرسم مرة أمام ومرة خلف

٥- نرقم المركبات في كل ايزومر من أكبر عدد ذري الى أصغر عدد ذري

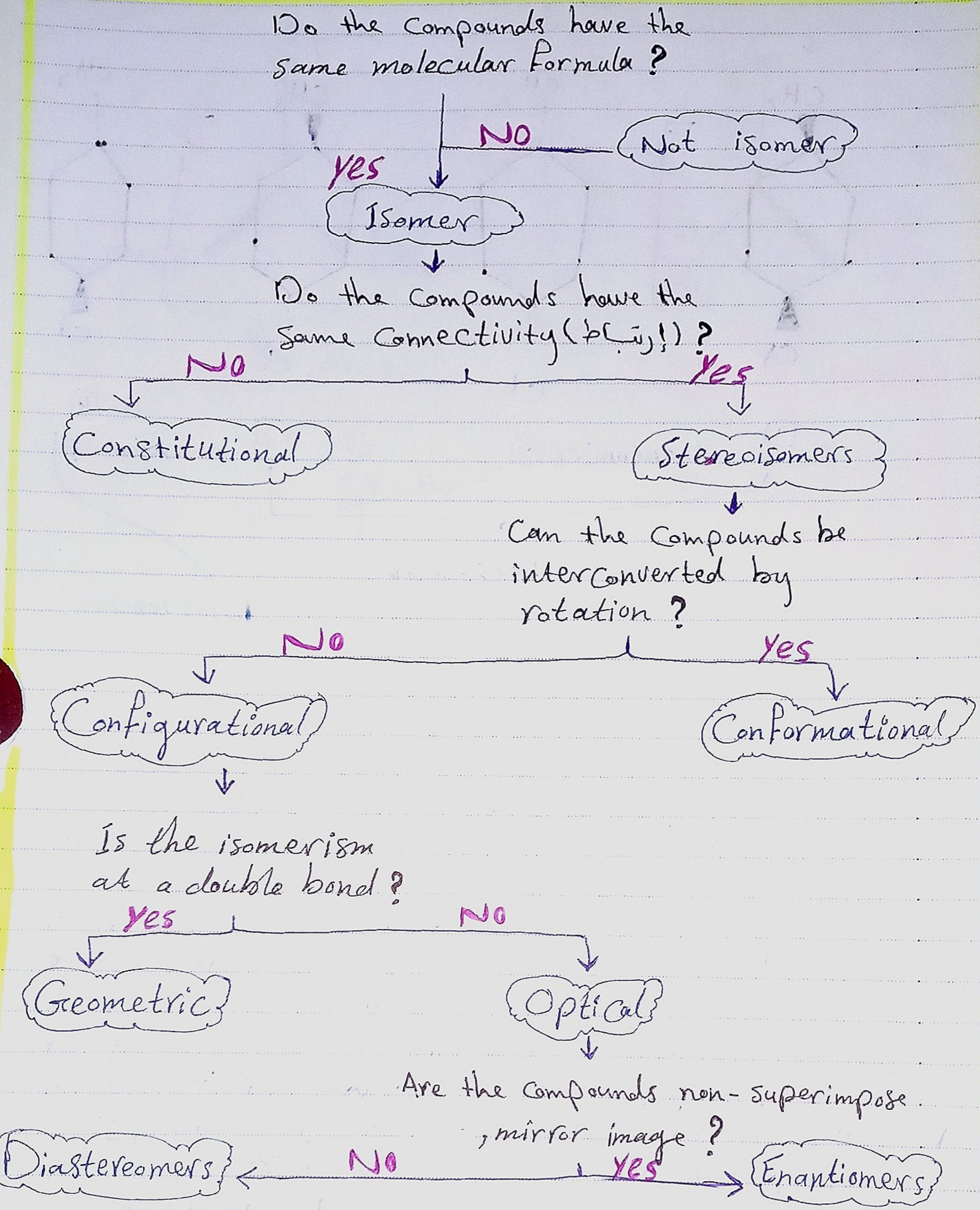
٦- إذا كان مع عقارب الساعة يسمى ⇐ R

٧- إذا كان عكس عقارب الساعة يسمى ⇐ S

٨- إذا اختلف ترتيب المركبات بحيث يكون كبير ← صغير ← كبير نعمل تشفت (⇅) فيكون الأصل S ولكن نحوله الى R

٩- أما في 2D لأنه يكون يمين و شمال فالرسم يكون متعامد بهذا الشكل + .

ALADIB


Do the compounds have the same molecular formula ?
NO
Not isomer
yes
Isomer
Do the compounds have the same connectivity (ترابط) ?
NO
Yes
Constitutional
Stereoisomers
Can the compounds be interconverted by rotation ?
NO
yes
Configurational
Conformational
Is the isomerism at a double bond ?
yes
NO
Geometric
Optical
Are the compounds non-superimpose, mirror image ?
NO
yes
Diastereomers
Enantiomers

11 / /

* Importance of stereochemistry :
- synthesis of drugs.

* Most drugs composed of :
- **active** stereoisomer, and another may be inactive
- active stereoisomer, and the other may be toxic
- active stereoisomer, and the other may be active.

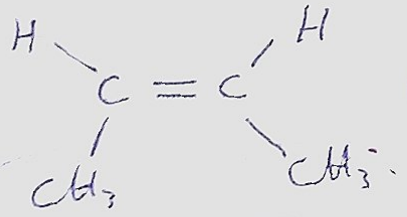
* Geometric [Cis - Trans] isomers result from restriction rotation.

Geometric

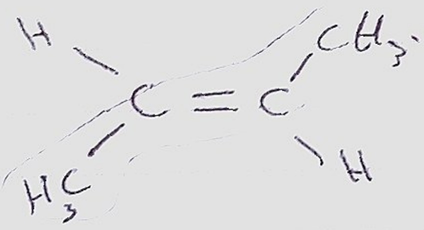
Double

- Cis ⇒ together (Z)
- Trans ⇒ opposite (E)

ex:



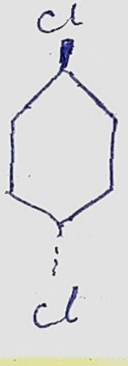
Cis = Z



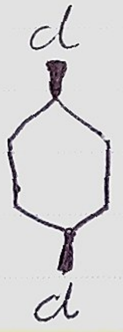
Trans = E

Ring

Cycloalkenes



Trans = E



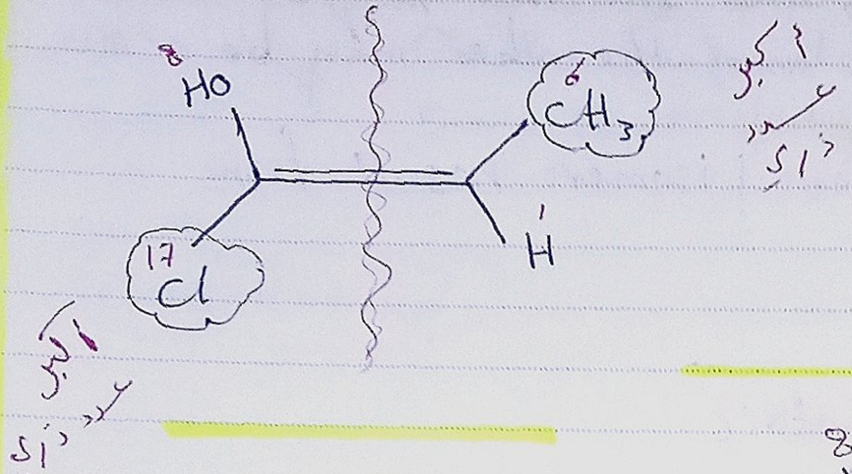
Cis = Z

٣

في حالة إذا اختلفوا المركبات في الأيزومرز (Cis-Trans) يتم تحديد Cis and Trans عن طريق :

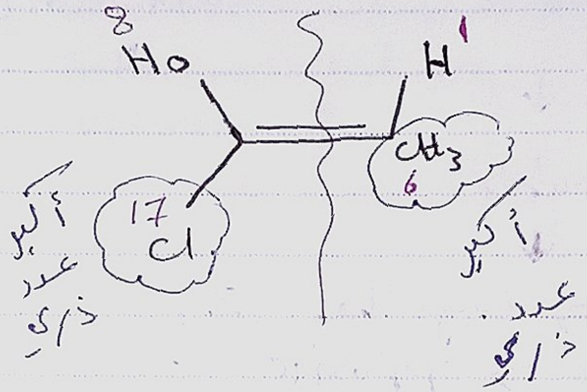
- تقسيم المركب إلى جزئين يمين وشمال
- البحث عن العدد الذري الأكبر للمركبات في كل جهة
- العدد الذري الأكبر هو يمثل (Cis - Trans)

مثال/


8
HO
6
CH3
1
H
17
Cl
أكبر عدد ذري
أكبر عدد ذري

⇒ Trans = E

Cis = Z ⇐


8
Ho
1
H
CH3
6
17
Cl
أكبر عدد ذري
أكبر عدد ذري

Cis isomer ⇒ The compounds are on the same side.

Trans isomer ⇒ The compounds are on the opposite side.

3

13 / /

Chiral	Achiral
- asymmetric	- symmetric
- stereocenter	- superimpose
- stereogenic center	- mirror image
- not superimpose	
- mirrore image	

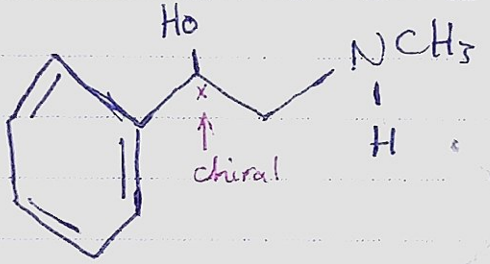
* Enantiomer ⇒ Mirror image , not superimpose

* Diastereomers ⇒ Not mirror image , not superimpose

كيف يتم معرفة إذا كان الدواء مفعول أم غير مفعول ؟

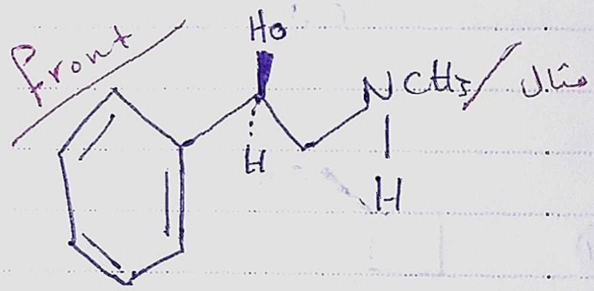
- إذا رسم الدواء على شكل } front and back or bold and dash

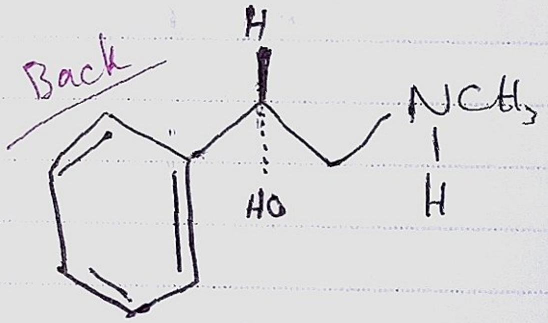
فيكون الدواء في هذه الحالة مفعول، والعكس.


Ho
NCH3
H
chiral

{غير مفعول}

مثال/


front
Ho
NCH3
H
H

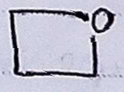
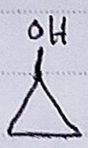

Back
H
NCH3
Ho
H

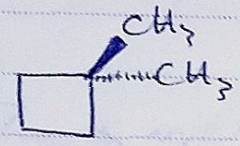
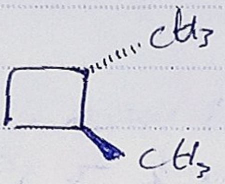
{مفعول}

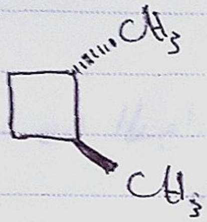
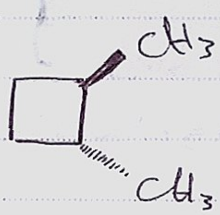
[3] ث 14 / /

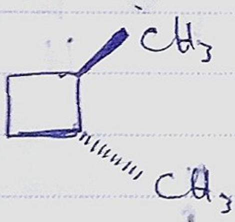
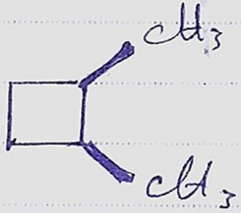
* Other importance of stereochemistry:
1- Increase receptors selectivity and potency.
2- Increase safety margin.
3- Decrease adverse effects of the drug.
4- Decrease dose given to the patient
5- Decrease the interaction of drug

ex:

①  and  ⇒ structural isomer

②  and  ⇒ structural isomer

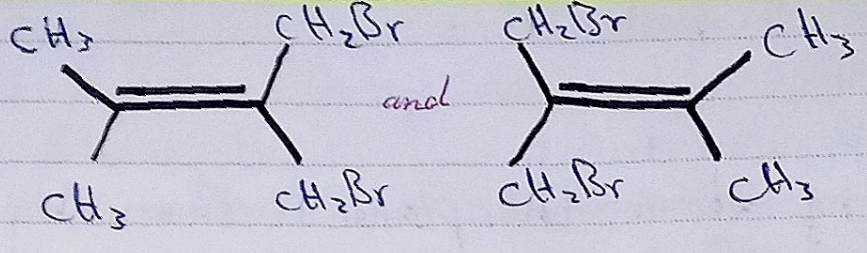
③  and  ⇒ enantiomer isomer

④  and  ⇒ diastereomer isomer

Examples

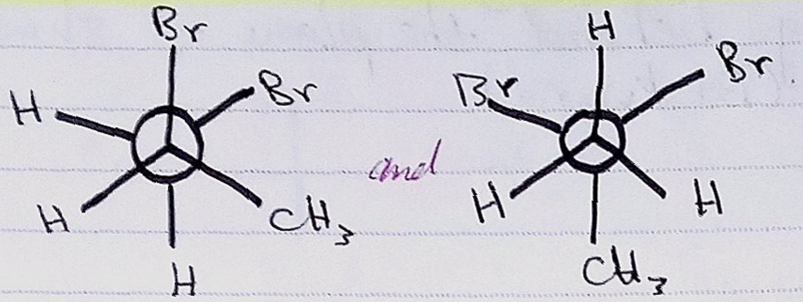
15 ; , ツ

⑤


CH₃
CH₂Br
CH₃
CH₂Br
and
CH₂Br
CH₃
CH₂Br
CH₃

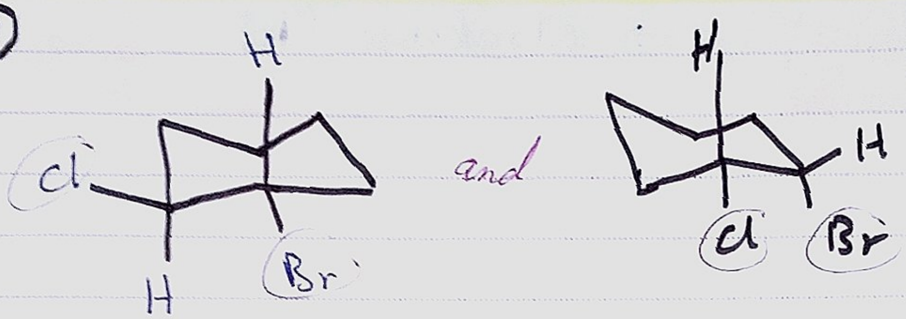
⇒ The same [Identical]

⑥


Br
H
Br
H
CH₃
H
and
H
Br
Br
H
H
CH₃

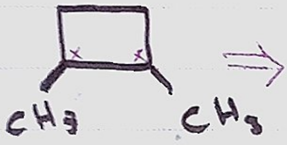
⇒ Structural

⑦


H
Cl
Br
H
and
H
H
Cl
Br

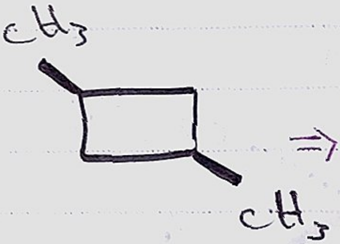
⇒ Cis-Trans

①



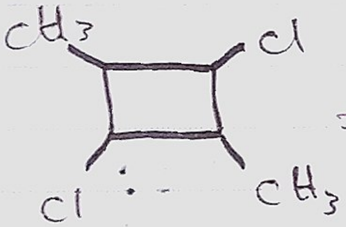
⇒ chiral

②



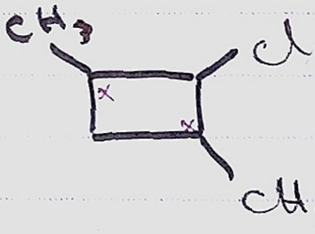
⇒ Achiral

③


CH₃
Cl
Cl
CH₃

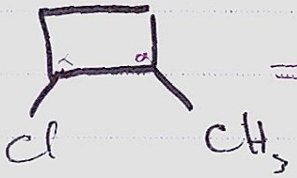
⇒ Achiral

④



⇒ chiral

⑤



⇒ Chiral

مينو الحضارة

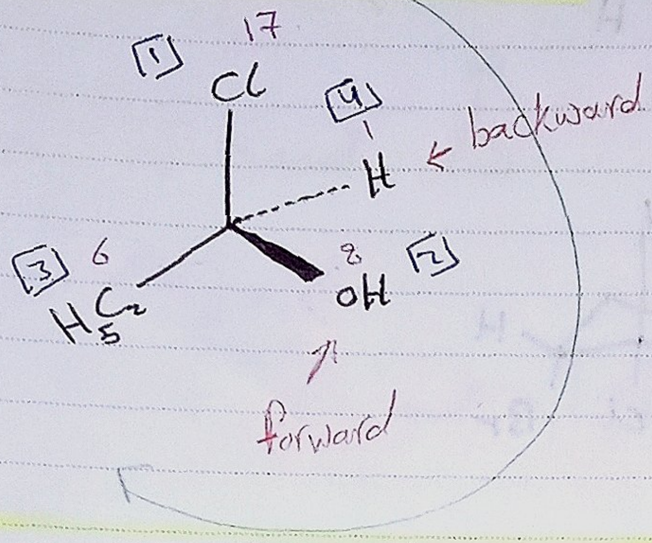
4

16 / 1 /

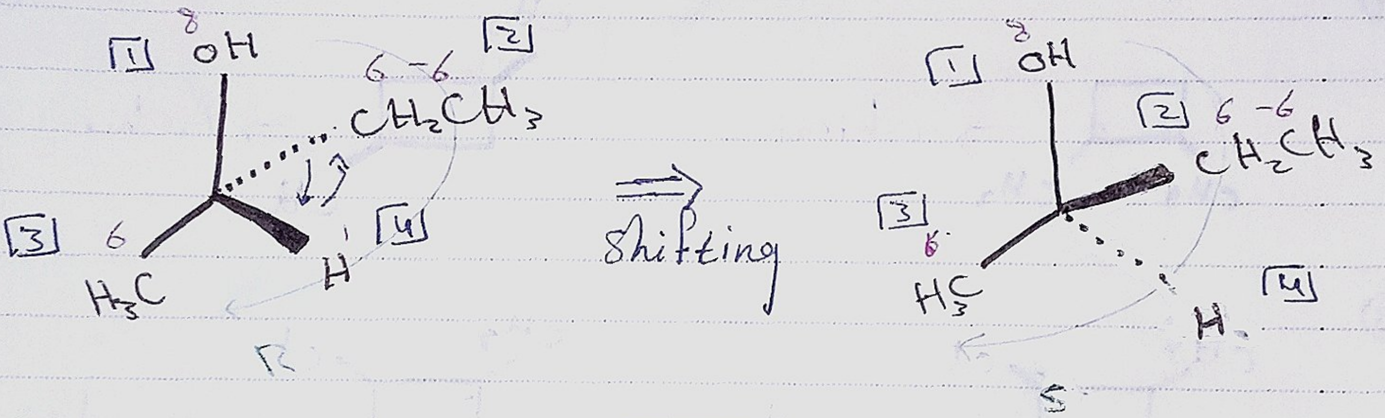
** Representation of molecule :-

1 Fly-wedge representation :-

- The atom pointing above the plane is shown by wedge line (forward)
- The atom pointing behind the plane is shown by dotted line (Backward)


17
1
Cl
4
1
H
backward
3
6
H_5C_2
8
OH
2
forward

⇒ clockwise (R)

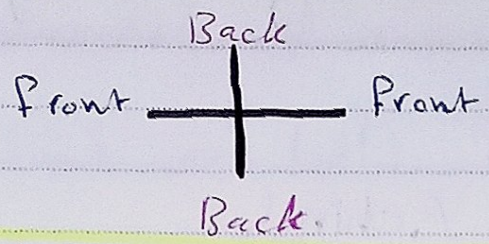

8
1
OH
2
6 -6
CH_2CH_3
3
6
H_3C
1
4
H
R
shifting
8
1
OH
2
6 -6
CH_2CH_3
3
6
H_3C
4
H
S

* متى نعمل شفت للـ fly-wedge ؟
- إذا لم تكن H في الخلف (dash)
- إذا لم تأخذ H أقل رقم في الترتيب

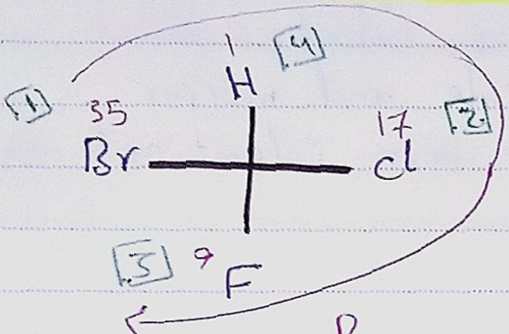
4 17 / /

2 Fischer projections representation :

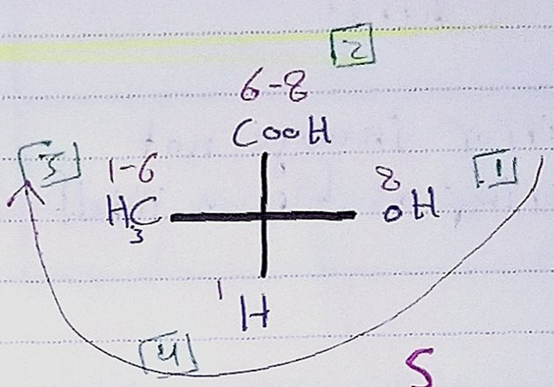
Shown by :
- Horizontal line is coming out of the plane.
- Vertical line is going back behind the plane.


Back
Front
Front
Back

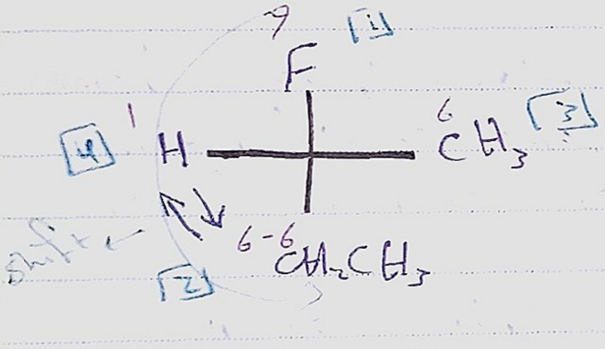
H ← تكون في back
وتأخذ أقل عدد ذري


1
H
4
1
35
Br
17
Cl
2
3
9
F

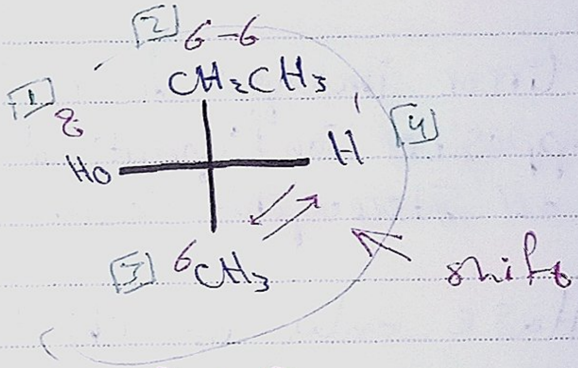
R


2
6-8
COOH
3
1-6
H_3C
8
OH
1
1
H
4

S


9
F
1
4
1
H
6
CH_3
3
shift
6-6
CH_2CH_3
2

S → R


2
6-6
CH_2CH_3
1
8
HO
1
H
4
3
6
CH_3
shift

R → S

✱ عندما نعمل shift ينعكس من R ← S أو S ← R

18/1

Conformer isomer	Configurational isomer
Interconvertible (قابل للتحويل) by rotation about single bonds	Not interconvertible by rotation, only by breaking & making bonds

Chiral	Achiral
Mirror image not superimposable on itself	Molecule and mirror image are identical

Enantimer	Diasteromers
- Mirror images; have opposite Configuration at all Stereogenic Center	Not mirror image; have the same configurations at one or more centers
- Hase only one chiral	- 2 chiral or more

Drugs	Glucose, amino acid (nature substances)
- Expermental ⇒ Dextro and levo ⇒ d or l + or −	- Expermental ⇒ d or l + or l
- Absolute ⇒ S or R Z or E	- Absolute ⇒ S or R, Z or E
	- Relative ⇒ D or L

* Racemic mixture (optical inactive) :-
is one that has equal amounts of enantiomers
(equal amounts of left - and right handed enantiomers)
of a chiral molecule.

* symbols of racemic mixture :-

(±) or (dl) or (RS and SR).

(DL) ⇒ for sugars.

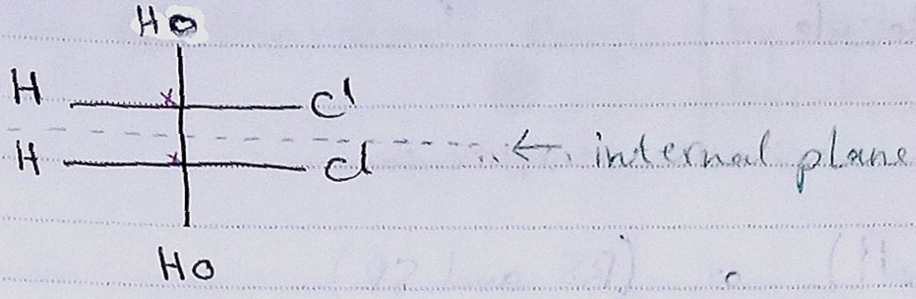
Racemic mixture doesn't rotate the light.

* Meso Compounds :-
- is a molecule with multiple stereocenters (chirals) that is superimposable on its mirro image.

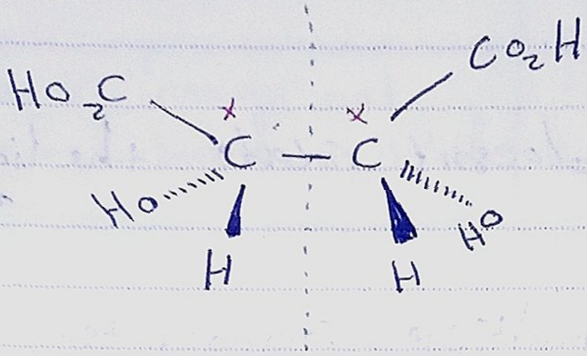
* properties of meso Compounds :-
① Has two chiral or more. and should be identical
② Is an achiral compound, but with chiral centers.
③ Optically inactive
④ Doesn't rotate the light.
⑤ no enantiomeric pair (mirror image & superimposable
⑥ has internal mirror plane through centers of molecules, that divide the compound in half.

* Examples of Compounds Contain an internal mirror plane of symmetry (Meso Compounds):

①


HO
H
Cl
H
Cl
HO
internal plane

②

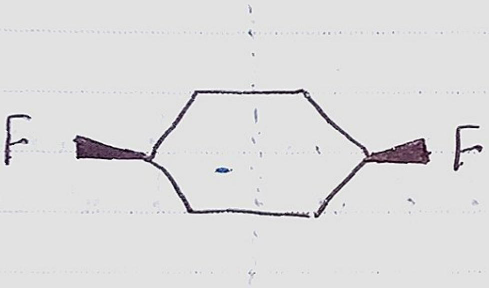

HO2C
CO2H
C
C
HO
HO
H
H

* 2 Chiral Center

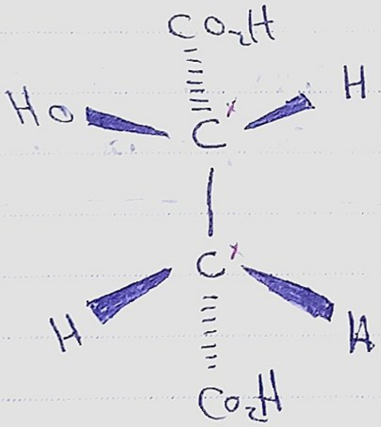
* الجهه اليمين
تساوي اليسار
أو الي فوق ينطبق
على الي تحت
يصبح achiral

فلا داعي للـ
Mirror image

③

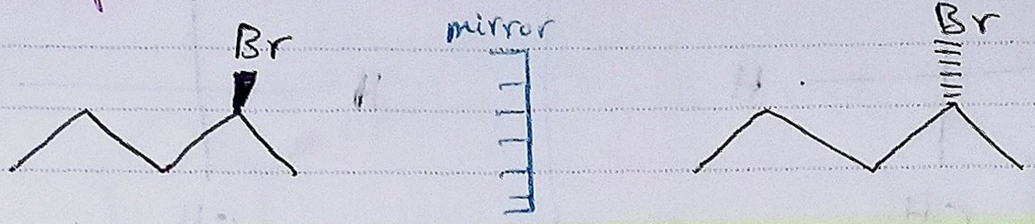


④

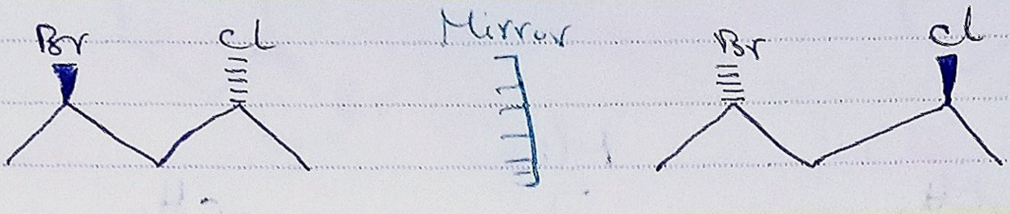

CO2H
HO
H
C
C
H
H
CO2H

* Eexamples of Enantimers :

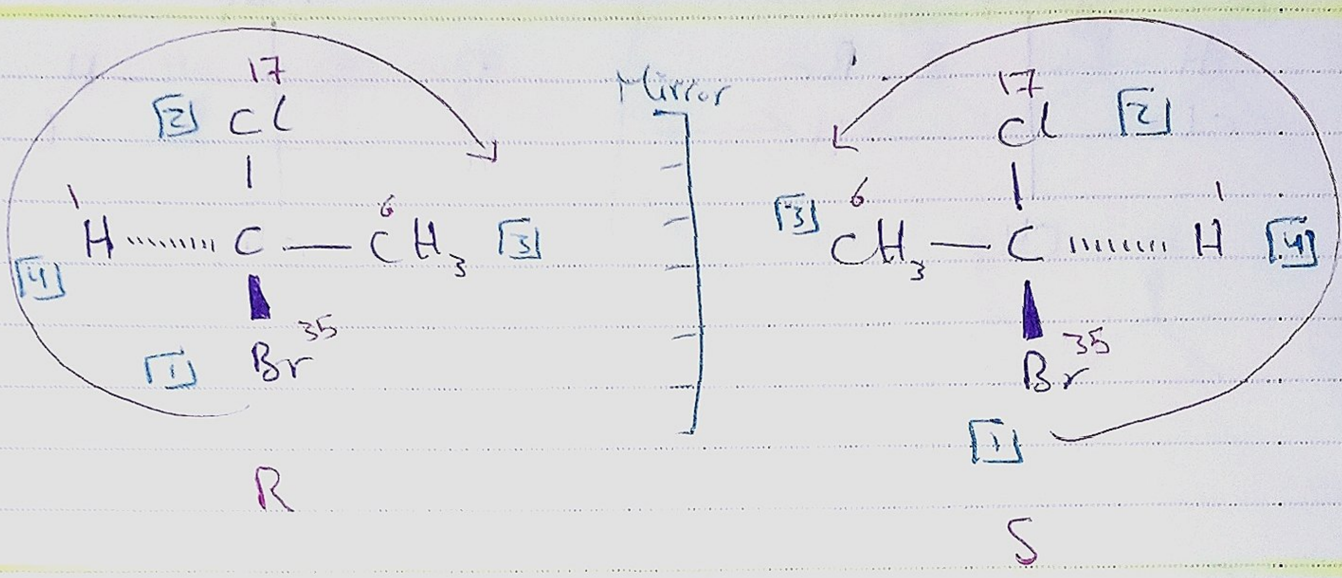
1


Br
mirror
Br

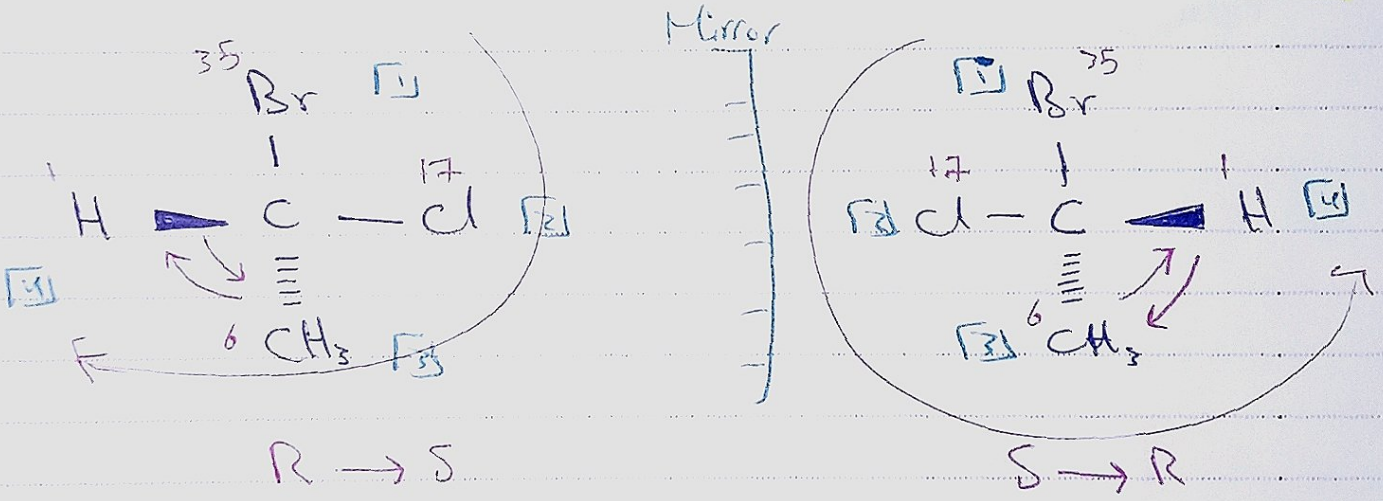
2


Br
cl
Mirror
Br
cl

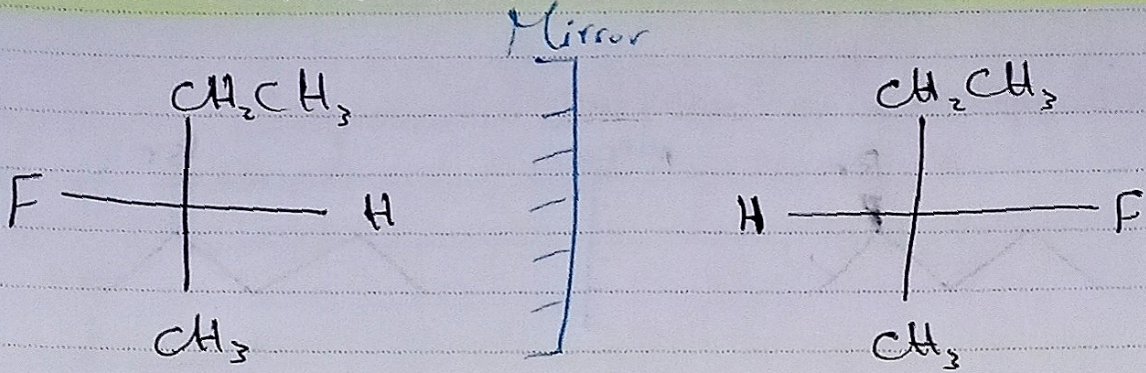
5


17
2 Cl
1
H
4
C
6
CH3
3
35
1 Br
R
Mirror
17
Cl 2
6
3 CH3
C
1
H 4
35
Br
1
S

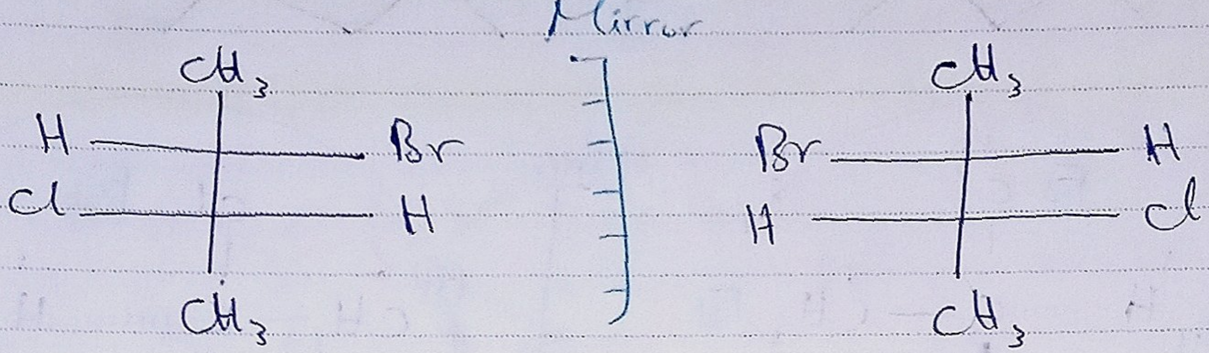
4


35
Br 1
1
H
4
C
17
Cl 2
6 CH3 3
R → S
Mirror
1 Br 35
17
3 Cl
C
1
H 4
3 6 CH3
S → R

⑤

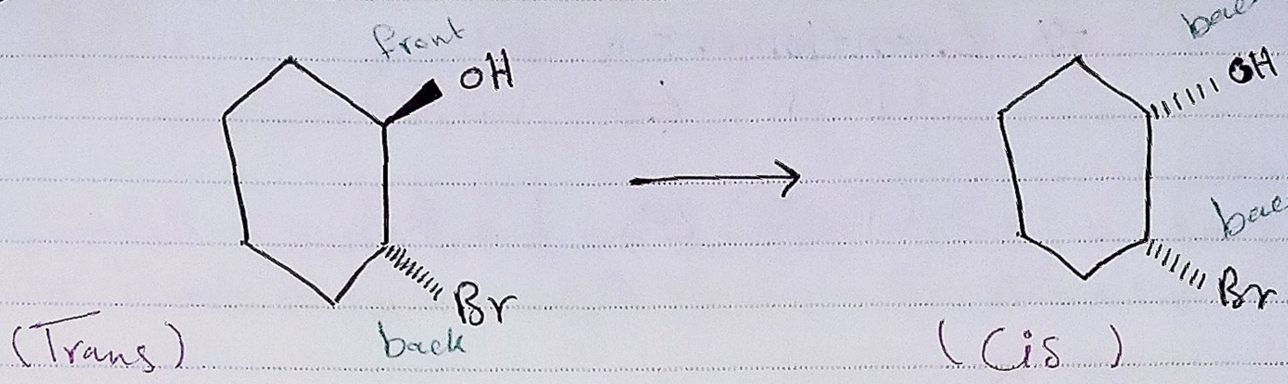

Mirror
CH_2CH_3
F
H
CH_3
CH_2CH_3
H
F
CH_3

⑥

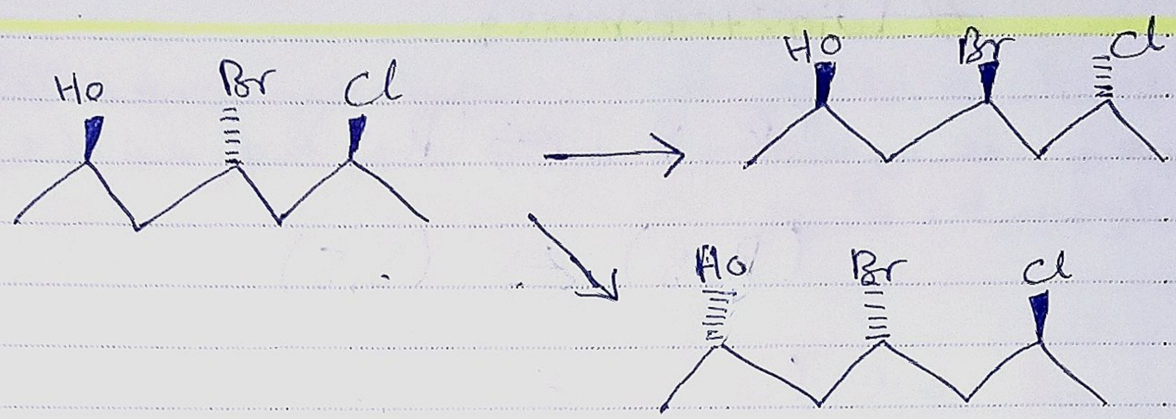

Mirror
CH_3
H
Br
Cl
H
CH_3
CH_3
Br
H
H
Cl
CH_3

* Examples of diastereomers :

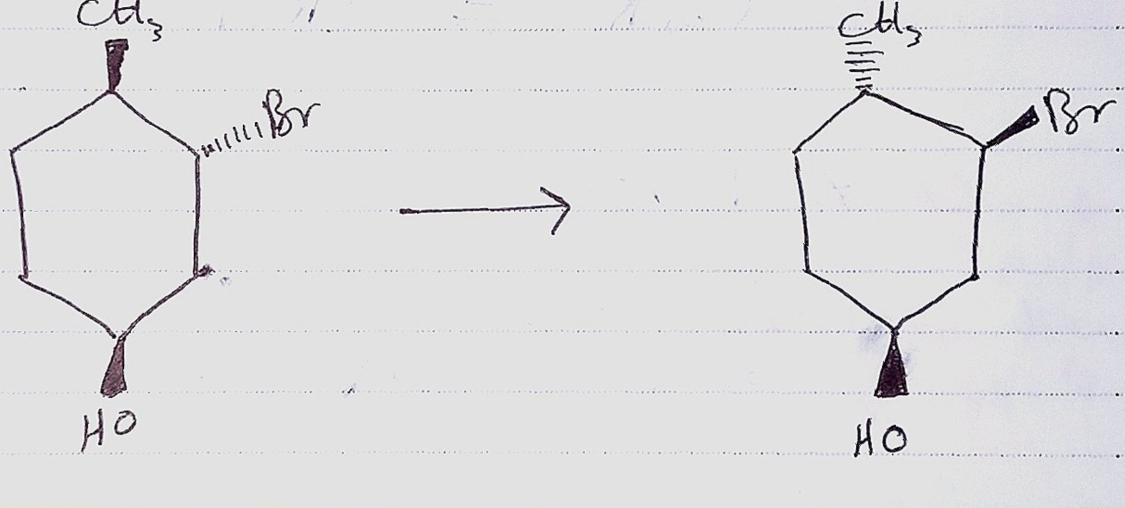
①


front
OH
Br
back
(Trans)
back
OH
back
Br
(Cis)

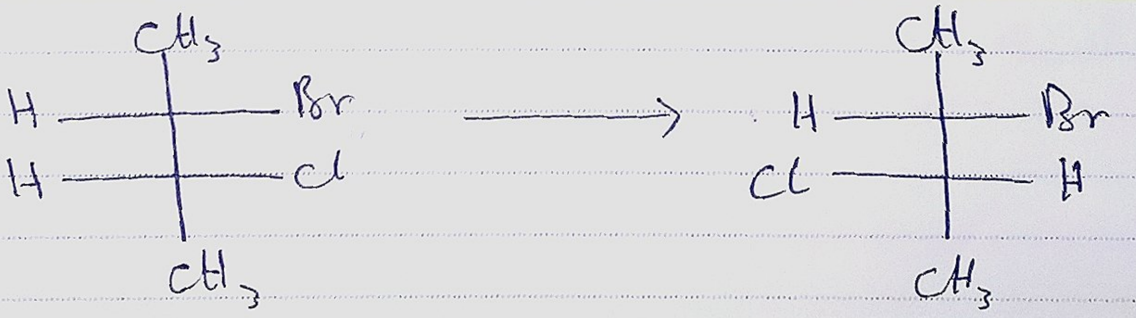
②


Ho
Br
Cl
HO
Br
Cl
Ho
Br
Cl

③


CH3
Br
HO
CH3
Br
HO

④


CH3
H
Br
H
Cl
CH3
CH3
H
Br
Cl
H
CH3

Enantiomers:

(R,R) ⇔ (S,S)

(R,S) ⇔ (S,R)

Diastereomers:

(R,R) ⇔ (R,S)

(R,S) ⇔ (S,S)

(S,S) ⇔ (S,R)

(S,R) ⇔ (R,R)

Meso:

If the same substances on both chiral atom

ALAVID.net صنو الحضارة

* كيف أحل الأختبار بدون ما ارتبش في الاختيارات ؟!

- في خطوات لازم نتبعها وهي كالتالي :

- أولاً :

في حالة إذا كانت المركبات مختلفة في الصيغة الكيميائية
بمعنى : مختلف في عدد ونوع الذرات ، تكون ⇐ Not isomer

- ثانياً :

في حالة إذا كانت المركبات معها نفس الصيغة الكيميائية
بمعنى : نفس عدد ونوع الذرات بغض النظر عن المجموعة
الوظيفية ، تكون ⇐ isomer.

- ثالثاً :

في حالة إذا كانت المركبات معها نفس الصيغة الكيميائية
ولكن مختلفة في الأسماء والخواص الفيزيائية والكيميائية
بمعنى : مركبات مختلفة ، تكون ⇐ Strucural.

- رابعاً :

في حالة إذا كانت المركبات معها نفس الصيغة الكيميائية
وأيضاً نفس الأسماء والخواص الفيزيائية والكيميائية ، ولكن
مختلفة في التوجيه ، واحد أمام والآخر خلف ،
تكون ⇐ Stereoisomers

- خامساً :

في حالة إذا كانت المركبات غير متطابقة ،
تكون ⇐ Optical.

- سادسة :

في حالة إذا كانت المركبات غير متطابقة ولكن صورة لبعض، مثل اليد، تكون ⇐ enantiomers

- سابعاً :

في حالة إذا كانت المركبات غير متطابقة وليست صورة لبعض، تكون ⇐ Diastereomers .

- ثامناً :

في حالة إذا كانت المركبات عبارة عن الكين (Double)، تكون ⇐ Geometric .

- تاسعاً :

في حالة إذا كانت المركبات Geometric ، وكانت في نفس الاتجاه، تكون ⇐ Cis (Z) ،

- عاشرة :

في حالة إذا كانت المركبات Geometric ، ولكن في اتجاهين متعاكسين، تكون ⇐ Trans (E)

- إحدى عشر :

في حالة إذا كانت المركبات enantiomers ، تكون

⇐ Racemic Mixture

- اثنى عشر :

في حالة إذا كانت المركبات Diastereomers ، تكون

⇐ Sepration

صنو الحضارة

- إذا وجدت كربونة معها اربع مجموعات متساوية ، تكون
  ⇐ Achiral

- إذا وجدت كربونة معها اربع مجموعات مختلفة ، تكون
  ⇐ Chiral

- كل Chiral معها ⇐ 2 isomers

- الـدبل يعتبر isomer ولكن لا يعتبر Chiral

- كل حلقتين متصلتين غير البنزين الكربونتين الي في الوسط
  تكون ⇐ chiral

صنو الحضارة

5 28 / /

① Stereoisomers with two asymmetric Carbons are Called ________ if the Configurational of both asymmetric Carbons in one isomer is the opposite of the Configuration of the asymmetric Carbons in the other isomer.

Ⓐ Diasteromers [✓ Ⓑ Enantiomers]
Ⓒ Meso Compounds Ⓓ non of the above.

---

② Stereoisomer with two asymmetric Carbons are Called ________ if the Configuration of both asymmetric Carbons in one isomer is the same as the Configuration of the asymmetric Carbons in the other isomer.

A- Diasteriomers B- enantiomers
[✓ C- meso Compounds] D- a and b

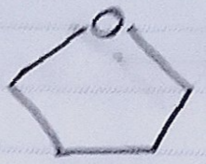
---

③ Stereoisomer with two asymmetric Carbons are Called ________ if one of the asymmetric Carbons has the same Configuration in both isomers and the other asymmetric Carbon has the opposite Configuration in the two isomers.

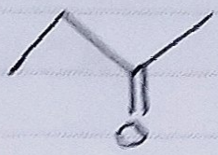
[✓ A- Diasteriomers] B- enantiomer
C- enantiomers D- meso Compounds

29, ,

④ Each pair of Compounds are ______ to each other :



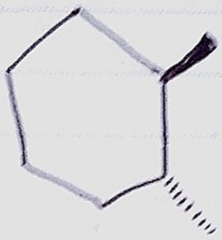
and



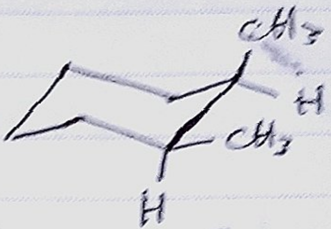
[✓ A- Structural isomer]
B- Stereoisomer
C- Not isomer

---

⑤ Each pair of Compounds are ______ to each other :



and

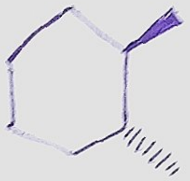


A- Structural isomer
[✓ B- Stereoisomer]
C- Not isomer

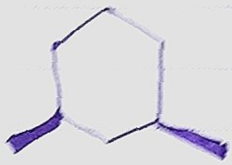
---

⑥ which of the following is meso Compounds :

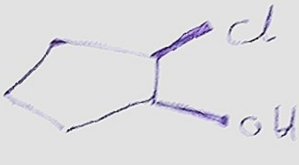
A-



[✓ B-]

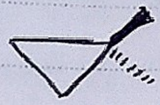


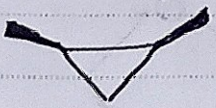
C-

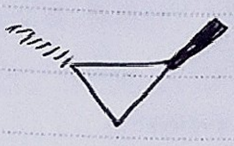


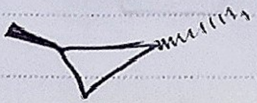
ALADIB

⑦ which Compounds are meso Compounds :

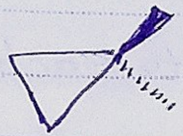
A-


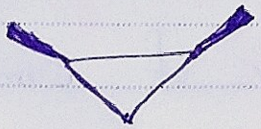
[✓ B-]


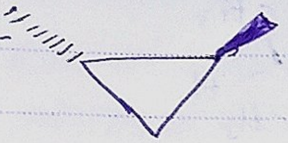
C-


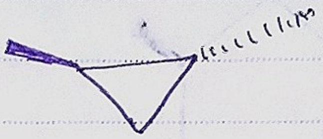
D-


⑧ which Compound are enantiomer Compounds :

A-


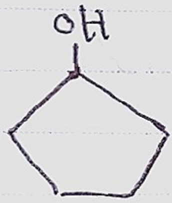
B-


C-


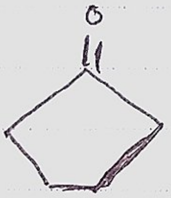
D-


A- A and B [✓ B- C and D] C- B and D

⑨ Each pair of Compounds are ______ to each other :



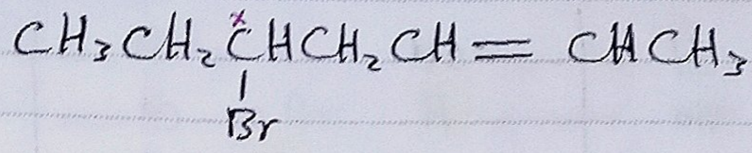
and



[✓ A- Structural isomer] B- Stereoisomer

C- not isomer

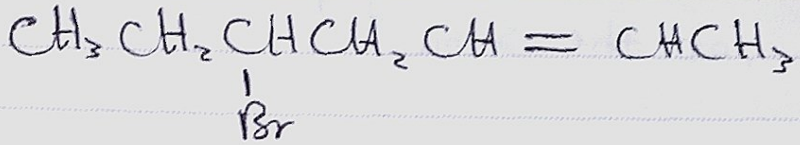
⑩ The following Compound has :-


$CH_3CH_2\underset{\underset{Br}{|}}{\overset{*}{C}}HCH_2CH=CHCH_3$

A- 2 isomer
B- 3 isomers
C- 4-isomers
D- None isomers

---

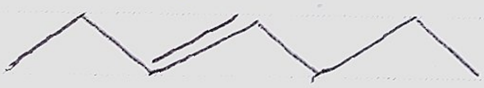
⑪ The following Compound has only one asymmetric Carbon, why then it have four isomers ?!

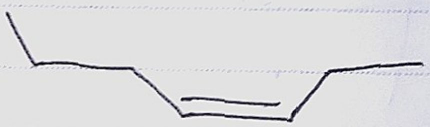

$CH_3CH_2\underset{\underset{Br}{|}}{C}HCH_2CH=CHCH_3$

A- Chiral
B- geometric
C- Conformation
D- Non of the above

---

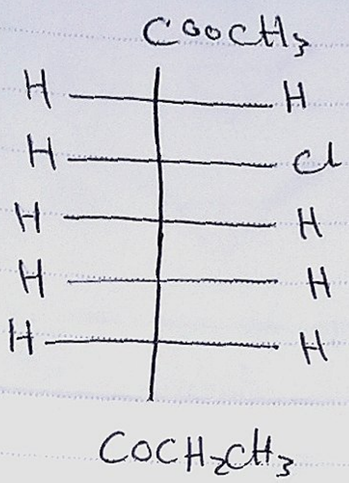
⑫ which of the following terms best describes the following pair of molecules ?!

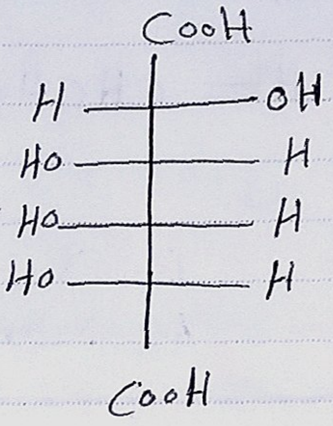


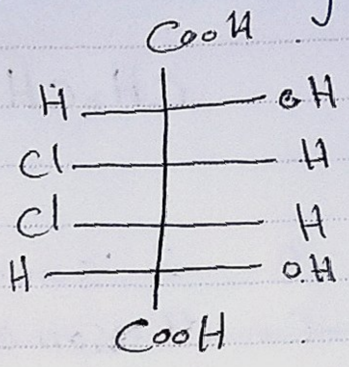


A- isomers
B- Constitutional isomer
C- Configuration isomer
D- Geometric isomer

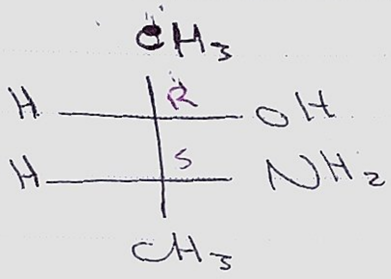
⑬ Which Compound will not exhibit optical activity?

A-

COOCH3
H
H
H
H
H
H
Cl
H
H
H
COCH2CH3

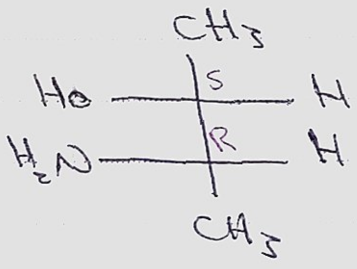
B-

COOH
H
HO
HO
HO
OH
H
H
H
COOH

C-

COOH
H
Cl
Cl
H
OH
H
H
OH
COOH

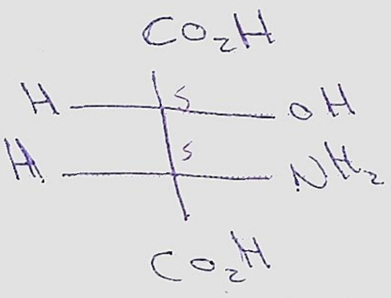
⑭ Classify each of the following pairs as: enantiomers, diastereomers, or the same.

[A]

CH3
H
H
R
S
OH
NH2
CH3

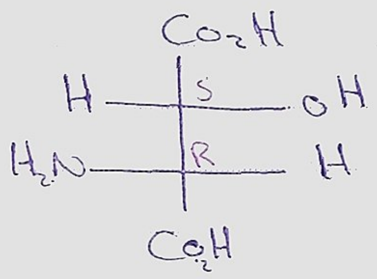
and


CH3
HO
H2N
S
R
H
H
CH3

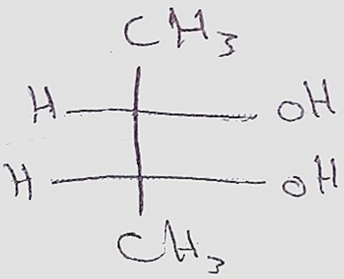
⇒ enantiomers

[B]

CO2H
H
H
S
S
OH
NH2
CO2H

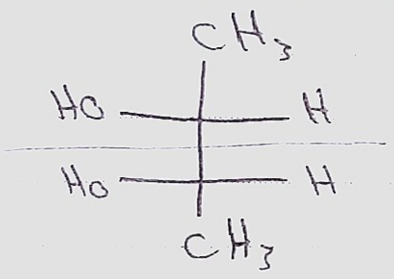
and


CO2H
H
H2N
S
R
OH
H
CO2H

⇒ diasteromers

[C]

CH3
H
H
OH
OH
CH3

and


CH3
HO
HO
H
H
CH3

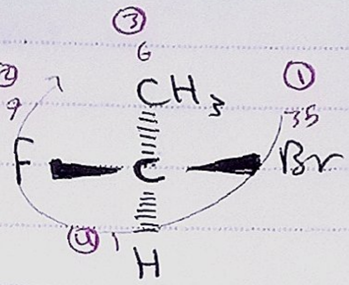
⇒ The Same

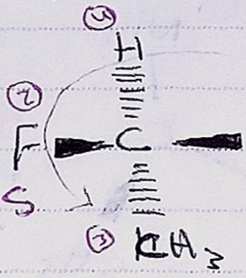
Meso: لا يعتبر

ALADIIB.net اصنع الحضارة

⑮ which of the following isomer is or are S conformer:

[1]

A-

③
6
CH3
②
9
①
35
F
C
Br
R
④
H

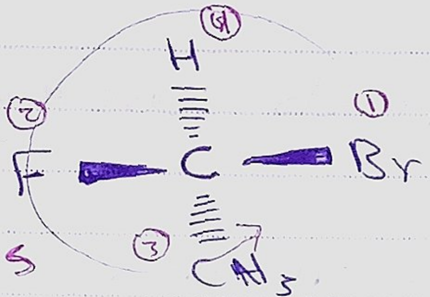
B-

④
H
②
①
F
C
Br
S
③
CH3

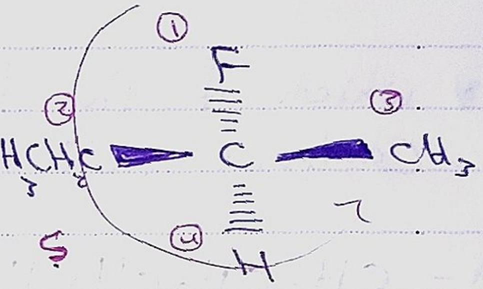
C- A and B

D- Non of the above.

---

[2]

A-

④
H
②
①
F
C
Br
S
③
CH3

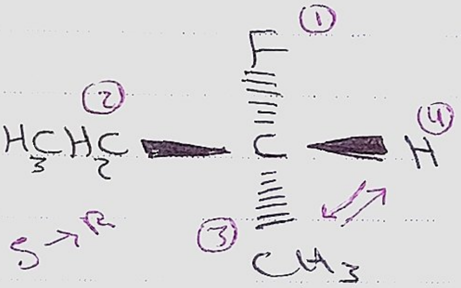
B-

①
F
③
③
H3CH2C
C
CH3
S
④
H

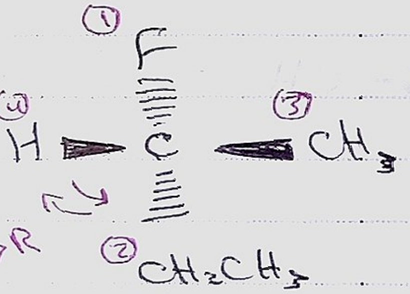
C- A and B

D- Non of the above

---

[3]

A-

①
F
②
H3CH2C
C
④
H
S → R
③
CH3

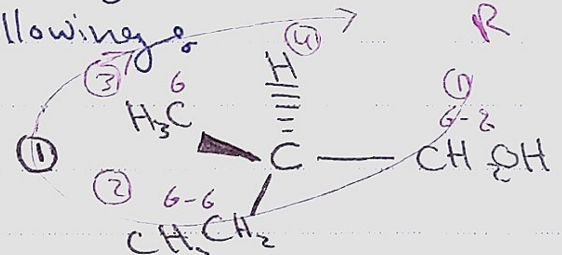
B-

①
F
④
H
C
③
CH3
S → R
②
CH2CH3

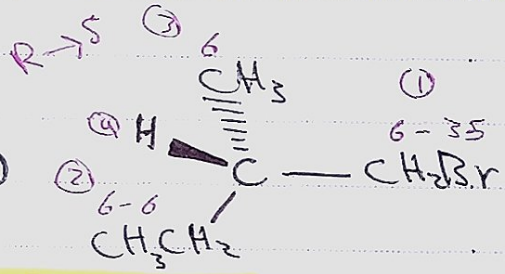
C- A and B

D- None of the above

---

⑯ Assign absolute configurations as R or S to the following:

①

④
H
R
③
6
H3C
①
6-8
C
CH2OH
②
6-6
CH3CH2

②

R → S
③
6
CH3
①
④
H
6-35
C
CH2Br
②
6-6
CH3CH2

A- 1=R , 2=R

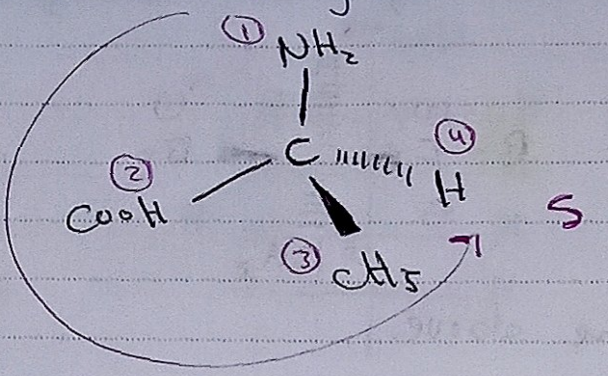
B- 1=R , 2=S

C- 1=S , 2=S

D- 1=1 , 2=R

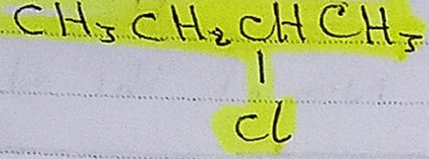
[17] Draw the S-configuration of $CH_3-CH(NH_2)-COOH$:

الحل :

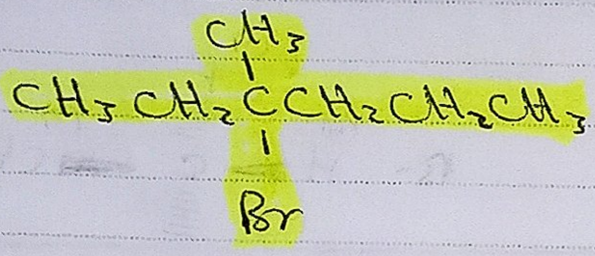

① NH_2
C
② COOH
④ H
③ CH_3
S

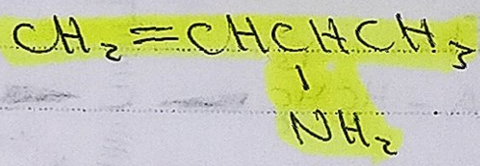
---

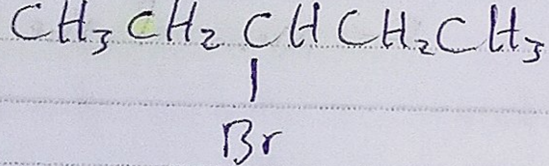
[18] which of the following Compounds have asymmetric Carbons (chiral) ?!

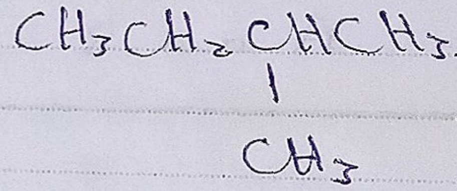
A -

$CH_3CH_2\underset{Cl}{\underset{|}{C}}HCH_3$

B - CH_3CH_2OH

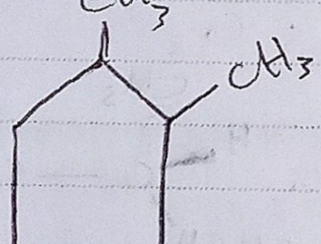
C -

$CH_3CH_2\overset{CH_3}{\overset{|}{\underset{Br}{\underset{|}{C}}}}CH_2CH_2CH_3$

D -

$CH_2=CH\underset{NH_2}{\underset{|}{C}}HCH_3$

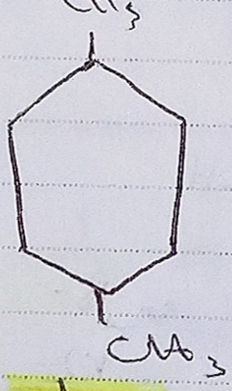
E -

$CH_3CH_2\underset{Br}{\underset{|}{C}}HCH_2CH_3$

F -

$CH_3CH_2\underset{CH_3}{\underset{|}{C}}HCH_3$

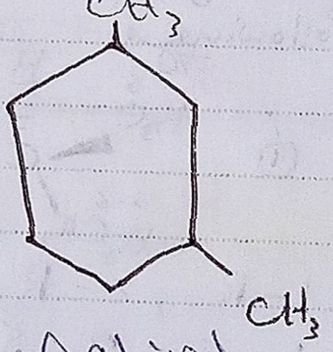
[illegible] -



Chiral.



Chiral



Achiral

صنو الحضارة

All the best

…